Approaches to Computational Modeling of Livestock Disease

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Collaborators (non-funded under this project):
Tom Bates, PhD (LLNL)
Mark Thurmond, PhD, Tim Carpenter, PhD (UC Davis)

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GOALS:

A. Evaluate existing computational approaches and efforts to model

- the introduction and spread of foreign animal diseases;
- strategies to control such epidemics; and
- the cost of foreign animal diseases epidemics

B. Design a large-scale decision support system to assist in

- tactical decision support: help experts in choosing optimal control strategies;
- contingency planning: explore hypothetical epidemics
- training of personnel: provide “virtual experience” in epidemics “combat”
- resource planning

BACKGROUND AND PREREQUISITES

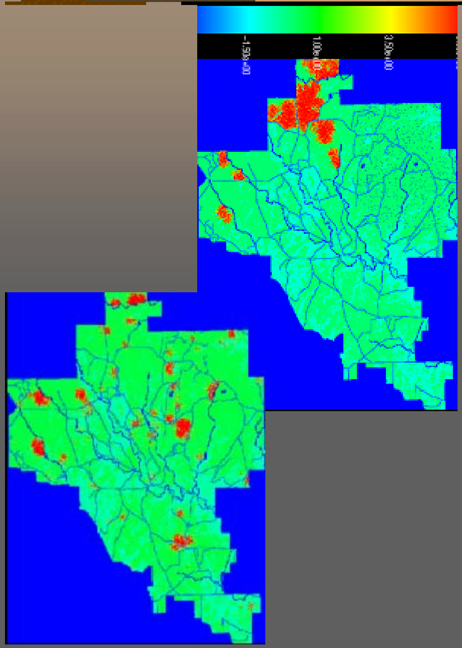
- Experience with individual-based spatially-explicit ecological simulations

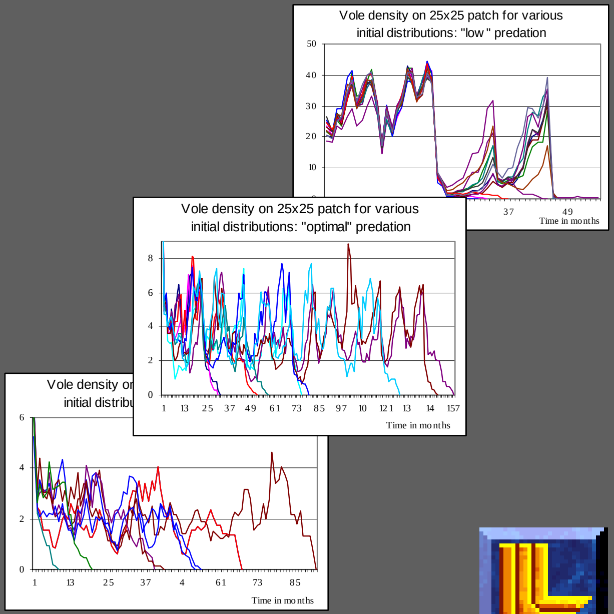
- Expertise in mathematical epidemiology (profound understanding of the existing methods and ideology)

- LLNL - natural environment for large scale modeling

- Collaborating with a team from UC Davis (T. Carpenter and M. Thurmond), (experts in FMD epidemiology, USDA FMD modeling grant, co-authors of California data-based FMD model)

- Possible collaboration with TAMU





Significance

Agriculture is a critical component of US economy

- Contribution of agriculture > $ 10^{12}/year
- Largest employer
- Export generated $5x10^9$/year

(Terry Wilson et al., *Clinics in Lab. Medicine* 2001)

Agriculture is vulnerable to bioterrorism

Targets: Livestock, crops, processed food, storage facilities

Production of livestock and livestock products are a substantial part of US agriculture

Significance

List A livestock diseases (Office International des Epizooties)

“Highly infectious, capable of rapid spread across borders, potential of catastrophic economic loss and social disruption”

Foot-and-mouth disease (FMD), avian flu, hog holera, Newcastle disease, emerging diseases...

An outbreak of a livestock disease such as FMD will lead to

losses measured in tens of billions of dollars

(loss of export markets, loss of livestock and livestock products)

Significance of the computational approach

Computational modeling can provide

• in-depth analysis and evaluation of disease spread (get insight, understand important components of process)

• estimate of timeline and scope of epidemic spread;

• source determination (methods to trace the source of the epidemic based on data and “predictor-corrector” modeling need to be developed)

Significance of the computational approach

Computational modeling can provide

- evaluate economic loss (models need to be populated with reliable data and improved estimates of the transmission rates)

- compare different control strategies (different epidemics require different combinations of strategies!)

- a method to differentiate between intentional and “by negligence” outbreak (?)

- virtual experience through training

Gaps

- No two epidemics are alike
- US livestock management practices have specific characteristics

➡ Direct application of existing foreign models is not recommended

- Detailed critical evaluation of existing models has not been done

Gaps

- Large-scale (state-wide and nation-wide) simulation capabilities need to be developed

- The cost and benefits of developing technologies for presymptomatic detection, sentinel methods and scenarios need to be evaluated.

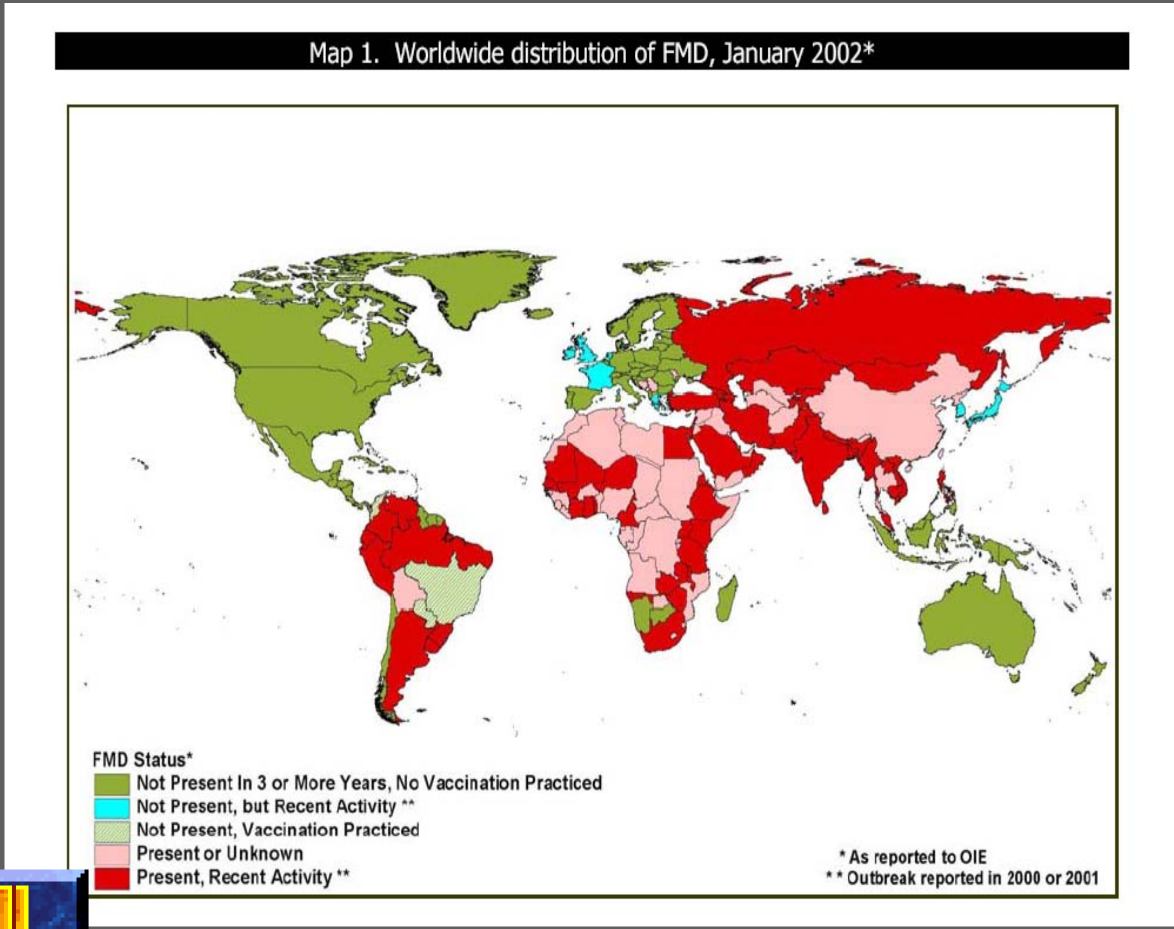
- Existing approaches from disciplines such as spatial ecology, mathematical epidemiology, immunological modeling, large-scale spatial simulations can and must be combined in the building of a large scale decision support tool.

But…

This work must be accompanied by the the development of livestock inventory database keeping track of animal, people and machinery movements between farms and of additional, more accurate epidemiological knowledge of disease transmission.

“FMD essentials”

FMD is considered the most economically disastrous list A disease;
FMD was eradicated in the US in 1929;
Recent epidemics UK 2001, Uruguay 2000



Report to US Congress, Prepared by the PL 107-9 Federal Inter-agency Working Group, January 2003

“FMD essentials” (Wilson et al. 2001, Sutmoller et al. *Virus Research* 2003)

Caused by the FMD virus (FMDV), family *Picornaviridae*, genus *Apthovirus*

- A highly adapted virus: low host mortality

- Airborne: (very small size, 25nm in diameter), can be carried by wind tens of miles; infects via a variety of routes, directly and indirectly

- 7 strains with different antigenic variation

- Virus stable at pH at low temperatures (<0ºC, indefinitely)

- Viability: 1 year in lab cultures at 4ºC, more than a month in soil

“FMD essentials”

- Multiple routes of infection

•Multiple hosts (cattle, pigs, sheep, goats, buffalo, wild animals; rats and mice are mechanical carriers)

• Different host species with different virus production rates, susceptibility thresholds, routes of infection, clinical symptoms, capacity as carriers

• A “sneaky” virus: infects before appearance of symptoms; infectious sheep and goats: mild symptoms, hard to detect

• Vaccines must match outbreak strain, <100% effective, protect 4-7 days post inoculation; immunity 6 months (max)

• Few studies focused on wild animals!

An “ideal” model should account for the complexity of the process

Should be spatially-explicit, as virus transmission has been found to depend on

- distance between an infectious source farm and susceptible farms
- size of a farm
- fragmentation of farm

GIS tools can be useful (roads, railways, natural barriers are important factors for infection route)

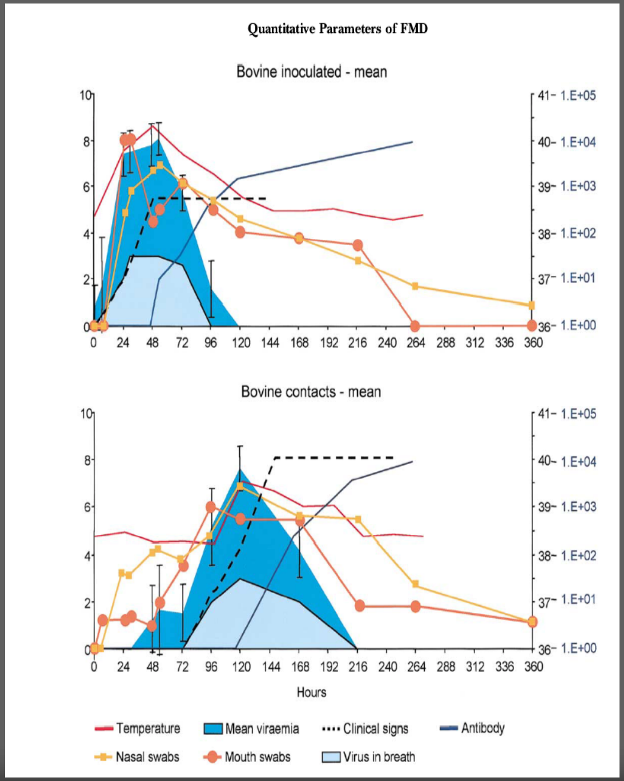
Important factors to be considered in a comprehensive model:

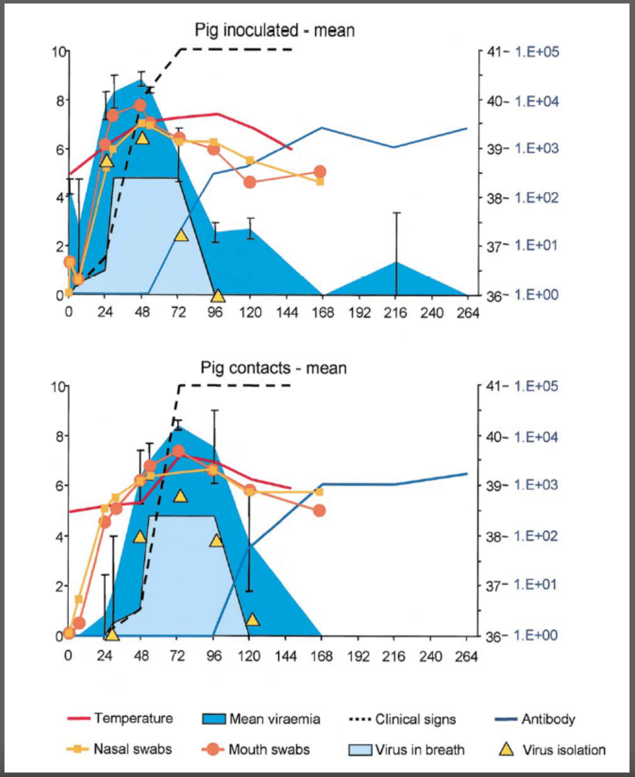
- Characteristics of virus strain (infectivity, aerosolization…)
- Individual animal information:

Species epidemic parameters (latent period, clinical signs period, infectiousness period, duration of immunity, …)

Average quantity and duration of virus production per animal from different species

First (published) accurate quantitative studies of virus production and excretion via different routes by different species would allow to estimate infectiousness of a herd





S. Alexandersen et al., J. Comp. Path. 2003

Important factors to be considered in a comprehensive model

- Individual farm characteristics of farm:

  Number of animals of different species

  Type of farm (milking, meat production, etc.) - defines quantity and type of indirect contacts

  Structure of farm: are species divided, how are animals handled (how many per pen, how many fed together, i.e. separate management groups)

  Number of people working on farm

Important factors to be considered in a comprehensive model

- Regional characteristics

  Spatial locations of farms, together with pastures used

  Distances between farms

  Locations of markets, slaughterhouses, other gathering points

  Distances between farms and gathering points

  Roads, railways

  Network information: common markets, transition centers, slaughterhouses, veterinarians, trucks, hoof-trimmers, farms belonging to one owner(and thus exchanging animals, materials)

Important factors to be considered in a comprehensive model

- Control-related parameters

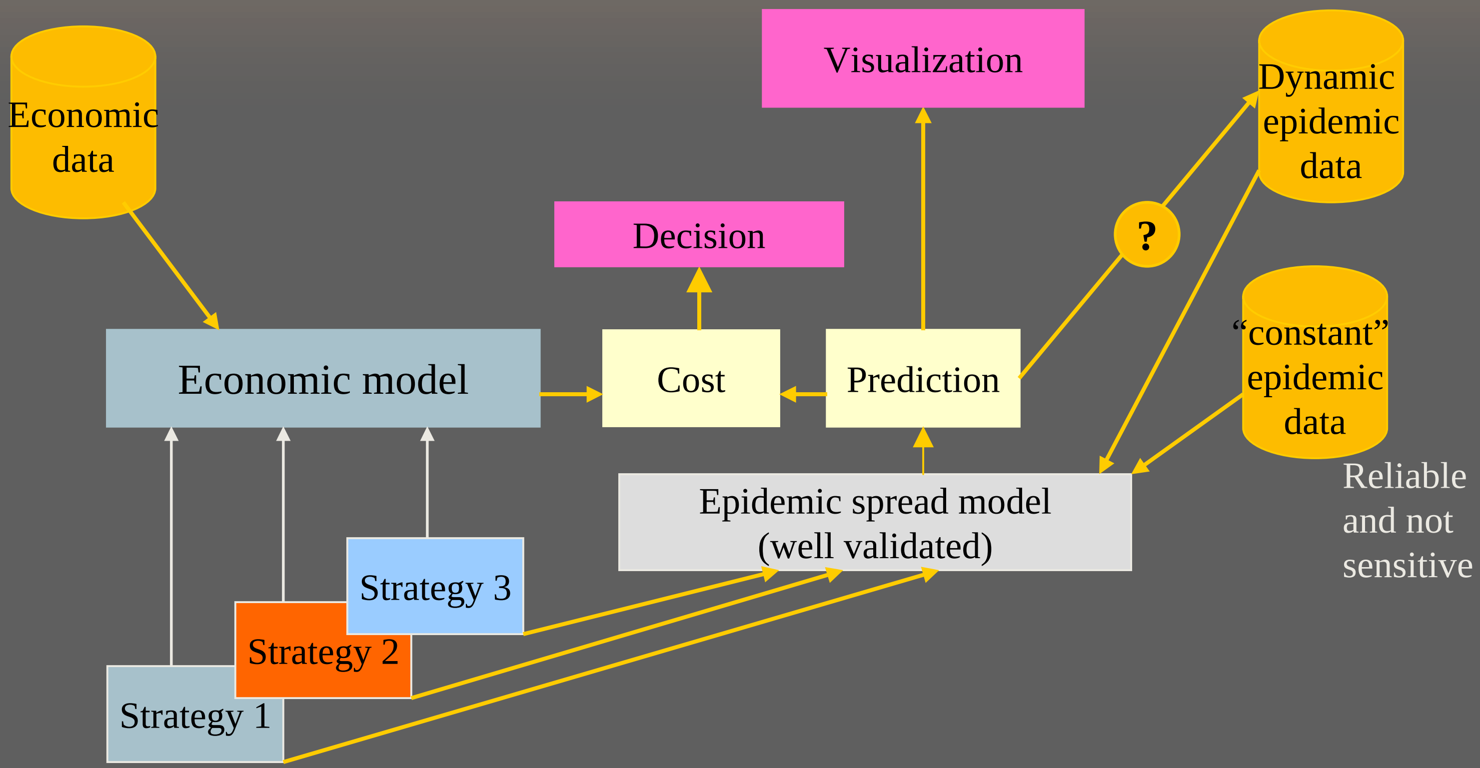
  Time since infection of farm

  Time between suspected infection and confirmed infection

  Time between confirmation and action

  Number of personnel available for vaccines, slaughter, etc. i.e. - an estimate how fast the strategies can be executed

Representation of model



Work completed so far

Bibliography of FMD modeling efforts and some epidemiological FMD epidemiological background reviews since 1990 assembled,
papers downloaded/ordered and received (about 80 titles)

Keeling, Science 2001

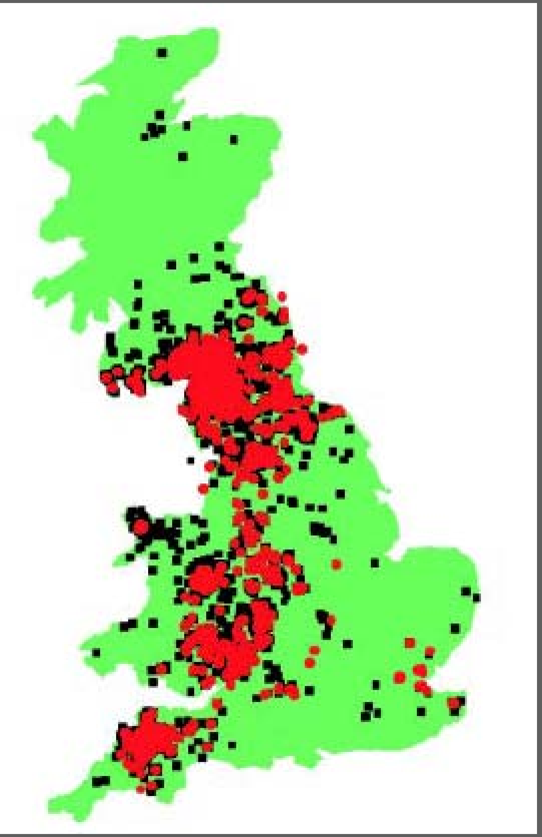
All modeling papers reviewed
Goal: write a critical review (with collaborators)

Short summary of models

All models use as an individual unit "the farm"

Common problem: how to evaluate transmission rates

Models after 2001 (UK epidemic) - spatial



Major Existing Models

Bates, Thurmond and Carpenter
"3-county model" based on real data for herd locations and sizes
Spatial stochastic simulation
Utilizes veterinary intelligence to create epidemiologic and other data;
Economic analysis, comparison of strategies
Intra-herd transmission module
Between herd transmission depends on distance, species susceptibilities; used to compare control strategies

Keeling et al.
Post-epidemic re-evaluation
of strategies including vaccination

Schoenbaum and Disney
Stochastic state transition model
Synthetic farm data, combined data from Bates et al. and other previous models
Economic analysis model

2001

Ferguson
deterministic ODE system
Non-spatial, one-species
Transmission represented as long and short range
model too abstract, lacking "veterinary intelligence"
Purpose: to evaluate strategies, UK policy largely based on it

Keeling et al.
Spatial, transmission rates depend on distance between farms, types of species in farm, numbers of animals from different species
Maximum likelihood fit
reconstructed roughly spatial spread
not very good end of epidemic prediction

EpiMan adapted to UK data
Predicted end of epidemic quite accurately
GIS incorporated, GUI

Haydon&Woolhouse
(simple deterministic discrete delay system): evaluates data of 1967-68 UK epidemic; evaluation of R_0 quite unrealistic

Garner&Lack
Stochastic state transition model
"spatial"
Transition rates stated to depend on many factors
but no details how included
Strategic scenarios

New Zealand's EpiMan (Morris, Sanson et al.)
Information System for disease control
Includes fully spatial, high complexity model InterSpread
Uses probability distributions from preassigned tables

Plume models

General observations

- None of the models is large-scale

- None of the models can be used in real-time epidemic (i.e. is adaptive and interactive)

- With the exception of Bates et al., none of the models incorporates intra-herd transmission

- Known network structure which would determine higher probabilities of transmission is not part of any model

PLAN

Q1/F04
Complete a review on existing models

Q2/F04
Develop requirements for large-scale model using the advantageous features of existing models; identify a specific problem to focus (depending on funding level)

Some obvious "niche problems":

- ✓ In-the-course-of-an-epidemic model: how to approach adaptive interactive modeling?
- ✓ A better intra-herd model
- ✓ Include network structure
- ✓ Include markets, gathering points
- ✓ Procedure to optimize manpower
- ✓ Graphical tool

Q1/F04
Initiate work on model/specific problem (depending on prospects for funding)

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